Niraparib Monotherapy

INDICATIONS FOR USE:

INDICATION	ICD10	Regimen Code	Reimbursement Status
As monotherapy for the maintenance treatment of adult patients with **platinum sensitive relapsed** -			CDS 1/3/2021
• high grade serous epithelial ovarian,	C56	00571a	
• fallopian tube or	C48	00571b	
• primary peritoneal cancer,	C57	00571c	
who are in response (complete response or partial response) to platinum-based chemotherapy			

TREATMENT:

The starting dose of the drugs detailed below may be adjusted downward by the prescribing clinician, using their independent medical judgement, to consider each patient's individual clinical circumstances.

Niraparib is taken once daily continuously until disease progression or unacceptable toxicity develops (1 cycle =28 days).

Drug	Dose	Route	Cycle
Niraparib	300mg[a] once daily	PO[b]	Continuous
[a]For patients <58kg a starting dose of 200mg may be considered			
[b]Capsules should be taken with or without food, swallowed whole with water and should not be chewed or crushed. Bedtime administration may be a potential method for managing nausea. If a patient misses a dose of niraparib, they should take their next dose at its scheduled time.			

ELIGIBILITY:

- Indications as above
- ECOG 0-1
- Histologically confirmed relapsed ovarian cancer, fallopian tube cancer, or primary peritoneal cancer
- High grade serous histology only
- Completed their latest platinum containing chemotherapy regimen in the previous 8 weeks.
- Completed at least two courses of platinum-based chemotherapy.
    - Following last regimen patients must have either
        1. CA125 in the normal range OR
        2. CA125 decrease by more than 90% during their last platinum regimen which is stable for at least 7 days (i.e., no increase >15%).
- Adequate haematological and organ function

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EXCLUSIONS:

- Hypersensitivity to niraparib or any of the excipients
- Pregnancy
- Breast-feeding during treatment and 1 month after the last dose

PRESCRIPTIVE AUTHORITY:

- The treatment plan must be initiated by a Consultant Medical Oncologist

TESTS:

Baseline tests:

- FBC, renal and hepatic profile
- Blood pressure
- A pregnancy test should be performed on all premenopausal women prior to treatment

Regular tests:

- FBC at 2 and 4 weeks followed by monthly monitoring for 1 year and then as clinically indicated
- Blood pressure should be monitored at 2 weeks, followed by monthly monitoring or as clinically indicated
- Renal and hepatic profile monthly

Disease monitoring:

Disease monitoring should be in line with the patient's treatment plan and any other test/s as directed by the supervising Consultant.

DOSE MODIFICATIONS:

- Any dose modification should be discussed with a Consultant.
- Treatment may be interrupted to manage adverse reactions. Dose reduction can be considered in these cases (Table 1).
- A starting dose of 200 mg for patients weighing less than 58 kg may be considered.

Table 1: Dose reduction for adverse events

Dose level	Dose Recommendation
Starting dose	300mg
Dose -1	200mg
Dose -2	100mg
Dose -3	Discontinue

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Haematological:

Table 2: Recommended dose modifications in haematological toxicity

ANC ($x10^9$/L)		Haemoglobin (g/dL)	Platelets ($X10^9$/L)	Dose
<1.0	Or	<8		• Withhold niraparib for a maximum of 28 days and monitor blood counts weekly until recovery (ANC ≥1.5x10^9/L or haemoglobin ≥9g/dL) • Resume niraparib at one reduced dose level • Discontinue niraparib if neutrophils and/or haemoglobin have not returned to acceptable levels within 28 days of the dose interruption period, or if the patient has already undergone dose reduction to 100 mg daily.
			< 100	*1st occurrence* • Withhold niraparib for a maximum of 28 days and monitor blood counts weekly until recovery to ≥100 x 10^9/L • Resume niraparib at same or reduced dose level based on clinical evaluation • If platelets < 75 x10^9/L at any time resume niraparib at one reduced dose level *2nd occurrence* • Withhold niraparib for a maximum of 28 days and monitor blood counts weekly until recovery to ≥100 x 10^9/L • Resume niraparib at one reduced dose level • Discontinue niraparib if the platelet count has not returned to acceptable levels within 28 days of the dose interruption period, or if the patient has already undergone dose reduction to 100mg daily.
Haematologic adverse reaction requiring transfusion or haematopoietic growth factor support				• For patients with platelet count ≤ 10 x 10^9/L, platelet transfusion should be considered. If there are other risk factors for bleeding such as co-administration of anticoagulation or antiplatelet medicinal products, consider interrupting these substances and/or transfusion at a higher platelet count. • Resume niraparib at a reduced dose.
Confirmed diagnosis of myelodysplastic syndrome (MDS) or acute myeloid leukaemia (AML)				• Permanently discontinue niraparib.

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Renal and Hepatic Impairment:

Table 3: Recommended dose modification in renal and hepatic impairment

Renal Impairment	Hepatic Impairment				
No dose adjustment is necessary for patients with mild to moderate renal impairment. There is no data in patients with severe renal impairment or end stage renal disease undergoing haemodialysis; use with caution in these patients		**AST**		**Total Bilirubin**	
	Mild	>ULN	and	≤ULN	No dose adjustment is needed.
		Any	and	1 – 1.5 x ULN	
	Moderate	Any	and	>1.5 – 3 x ULN	Recommended dose 200mg once daily.
	Severe	Any	and	>3 x ULN	There is no data in patients with severe hepatic impairment; use with caution in these patients.

Management of adverse events:

Table 4: Recommended dose modifications for adverse reactions

Adverse Reaction	Dose Modification
≥ Grade 3* treatment-related adverse reaction where prophylaxis is not considered feasible or adverse reaction persists despite treatment	*1st occurrence* • Withhold niraparib for a maximum of 28 days or until resolution of adverse reaction. • Resume niraparib at one reduced dose level *2nd occurrence* • Withhold niraparib for a maximum of 28 days or until resolution of adverse reaction. Resume niraparib at one reduced dose level
≥ Grade 3* treatment-related adverse reaction lasting more than 28 days while patient is administered niraparib 100mg/day	Discontinue treatment

*CTCAE=Common Terminology Criteria for Adverse Events

SUPPORTIVE CARE:

EMETOGENIC POTENTIAL: Low **(Refer to local policy)**.

PREMEDICATIONS: None recommended

OTHER SUPPORTIVE CARE: No specific recommendations

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ADVERSE EFFECTS / REGIMEN SPECIFIC COMPLICATIONS:

Niraparib is subject to additional monitoring. Healthcare professionals are asked to report any suspected adverse reactions. *The adverse effects listed are not exhaustive. Please refer to the relevant Summary of Product Characteristics for full details*.

- **Haematologic toxicity**: Haematologic toxicity (thrombocytopenia, anaemia, neutropenia) has been reported in patients treated with niraparib. If a patient develops severe persistent haematologic toxicity including pancytopenia that does not resolve within 28 days following interruption, niraparib should be discontinued. If a patient develops severe persistent haematologic toxicity that does not resolve within 28 days following interruption, niraparib should be discontinued. Due to the risk of thrombocytopenia, anticoagulants and medicinal products known to reduce the thrombocyte count should be used with caution.
- **Myelodysplastic syndrome/acute myeloid leukaemia**: Cases of Myelodysplastic syndrome/acute myeloid leukaemia (MDS/AML) have been reported in clinical studies with niraparib. If MDS and/or AML are confirmed while on treatment with niraparib, treatment should be discontinued and the patient treated appropriately.
- **Hypertension:** Hypertension, including hypertensive crisis, has been reported with the use of niraparib. Pre-existing hypertension should be adequately controlled before starting niraparib treatment. Blood pressure should be monitored monthly for the first year and periodically thereafter during treatment with niraparib. Hypertension should be medically managed with antihypertensive medicinal products as well as adjustment of the niraparib dose. Niraparib should be discontinued in case of hypertensive crisis or if medically significant hypertension cannot be adequately controlled with antihypertensive therapy.
- **Posterior reversible encephalopathy syndrome (PRES):** There have been reports of Posterior Reversible Encephalopathy Syndrome (PRES) in patients receiving niraparib. In case of PRES, it is recommended to discontinue niraparib and to treat specific symptoms including hypertension. The safety of reinitiating niraparib therapy in patients previously experiencing PRES is not known
- **Pregnancy/contraception:** Niraparib should not be used during pregnancy or in women of childbearing potential not willing to use reliable contraception during therapy and for 1 month after receiving the last dose of Niraparib. A pregnancy test should be performed on all women of childbearing potential prior to treatment.
- **Lactose**: Niraparib hard capsules contain lactose monohydrate. Patients with rare hereditary problems of galactose intolerance, the Lapp lactase deficiency or glucose-galactose malabsorption should not take this medicine.
- **Tartrazine (E 102):** This medicinal product contains tartrazine (E 102), which may cause allergic reactions.

DRUG INTERACTIONS:

- Current drug interaction databases should be consulted for more information.

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2. Mirza MR et al. Niraparib Maintenance Therapy in Platinum-Sensitive, Recurrent Ovarian Cancer. N Engl J Med. 2016 Dec 1; 375(22):2154-2164. doi: 10.1056/NEJMoa1611310. Including supplementary material.
3. Berek et al. Safety and dose modification for patients receiving niraparib. Annals of oncology 29:1784-1792, 2018

Version	Date	Amendment	Approved By
1	01/03/2021		Dr Dearbhaile Collins
2	08/07/2021	Update of hepatic dose modifications as per SPC update	Dr Dearbhaile Collins

Comments and feedback welcome at oncologydrugs@cancercontrol.ie.

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